

Music Therapy Modulates Combined Predator and Noise Stress Induced Anxiety-Like Behavior in Male Wistar Rat

*Nawel Attoui, Imed Eddine Bouhali, Hakima Tayaa,
Wafa Habbachi, Abdelmadjid Bairi and Abdelkrim Tahraoui*

Applied Neuroendocrinology Laboratory, Department of Biology,
Faculty of Science, University Badji Mokhtar 23000, Annaba, Algeria

Abstract: Exposure to music episodes is considered among the methods used in therapy. In our work, stressed rats by combined predator and noise stress for seven consecutive days displayed increase in the level of plasma ACTH and anxiety behavior, besides; Post-exposure to classical music of Mozart reduced efficiently the changes related-stress. Notably, Use music in life seems to be beneficial to alleviate negative outcomes of stress.

Key words: Stress • Predator • Noise • Music • Rat

INTRODUCTION

Stress is constant in our lives and cannot be avoided [1]. It is known to induce alterations in various physiological and behavioral responses even leading to pathological state [2]. Stress is a biologically significant factor that, by altering brain cell properties, can disturb cognitive and consequently limit the quality of human life [3]. According to the original stress concept, introduced by Selye [4] and Cannon [5], stress was thought to be a non-specific response to stressors always inducing the activation of adrenal glucocorticoid and catecholamine release. Substantial stressor specificity has been demonstrated in the activation of the HPA axis and sympathoadrenal system, known to be the main stress systems in both humans and experimental animals [6]. Predator and noise stress are among models stress used in experimental studies [7, 8]. Both stress induce intense stimulation of HPA axis and are related behavioral pathologies.

Negative outcomes of stress lead researchers to investigate many methods of therapy and prevention. Recently, a great attention was paid to music having power to modulate stress responses. Soothing effects of music on human psychology and behavior are well known [9]. Classical music also appears to influence the behavior

and/or physiology of captive animals in a manner suggestive of enhanced well-being [10]. In addition; other studies show that music leads to positive behaviors [11] and physiological benefits [12]. The value of auditory enrichment has been studied in a variety of species, including birds [13]. In this work, we attempted to investigate the effect of music on combined predator and noise stress induced behavioral and hormonal changes in male Wistar rat.

MATERIALS AND METHODS

Experimental Protocol: Male Wistar rats obtained from Pasteur Institute (Algiers, Algeria) were housed in transparent cages at a constant temperature (23 ± 1 °C) with a 12 h/12 h light/dark cycle (Lights on at 07:30 a.m.). Rats had access to standard rodents chow and tap water *ad libitum* and weighing 240 ± 30 g at the beginning of the experiment. Rats were divided into 08 groups each of 08 rats; Control group (C), Noise stress group (N), Predator stress (P), Predator + Noise stress group (PN), Music group (M), noise stress + music group (NM), Predator stress + Music group (PM), combined noise and Predator stress + Music (PN+M). In predator stress, rats were exposed to the odor of collar cat for 10 min for 7 days; In noise stress: rats were exposed to the Klaxon of 105 dB

for 10 min for 7 days; in music group: rats exposed to classical music for 10min after application of stress. Symphony of Mozart was selected in this music therapy« n°5in B flat Major, K22 ».

Elevated Plus-Maze Test: The elevated plus-maze (EPM) test is a widely used paradigm to investigate anxiety-related behavior in rats [14]. The EPM was made of painted wood cross (Arms 50 cm long x 10 cm wide) elevated 50 cm above the floor. Two opposite arms were enclosed by walls (10 cm x 50 cm x 45 cm high) and two arms were open. The arms extended from a central platform (10 x 10 cm) [15]. The open arms in the maze that we use do not have a railing, but addition of a 3-5 mm high railing on the open arms of the plus maze has been used with success to increase open arm exploration. The rat was placed in the center of the apparatus facing one of the open arms, for a free exploration of 5 min. Entry into an arm was defined as the animal placing all four paws on the arm. After each test, the rat was returned to its home cage and the maze was cleaned with an alcoholic solution followed by wet and dry paper towels, prior to the next trial. Time spent in open and closed arms was measured.

Level of Plasma ACTH: After behavioral testing, rats were decapitated and the blood collected in EDTA tubes. After centrifugation, Plasma samples were used to determine ACTH concentration by chemiluminescent method using IMMULITE.

Statistical Analysis: XLStat 2009 was used for statistical analysis. All data are presented as mean ± SEM. The data obtained were tested student test. $P < 0.05$ was considered statistically significant.

RESULTS

Effect on ACTH Level: Exposure to different forms of stressors alone or in combined form increase significantly ($p < 0.001$) ACTH secretion. However, post-exposure with music decrease the secretion of ACTH in all groups, however, significant difference to control ones remains detected.

Effect on the Time of Spent in Open Arms: Exposure to odor of cat decrease significantly the time spent in open arms, mainly in the combined stress group ($p < 0.001$). Post-exposure to music increase this time as like in control ones.

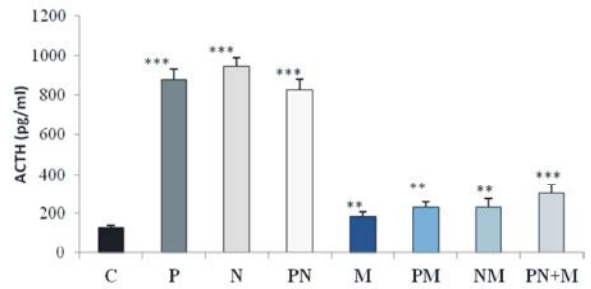


Fig. 1: Effect of music on ACTH variation in stressed groups. (n=08, * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$)

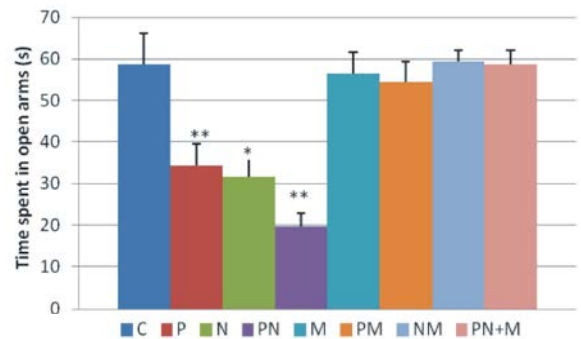


Fig. 2: Effect of music on the time spent in open arms in stressed groups.. (n=08, * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$)

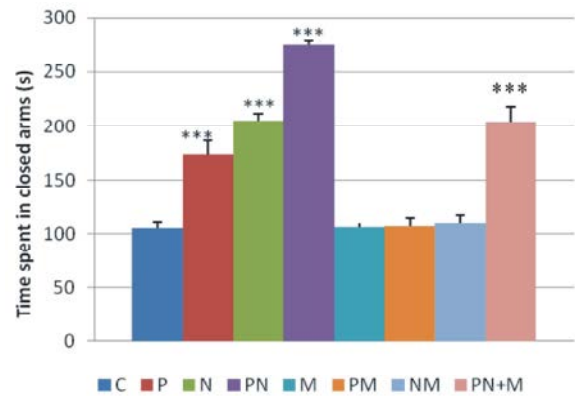


Fig. 3: Effect of music on the time spent in closed arms in stressed groups.. (n=08, * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$)

Effect on the Time of Spent in Closed Arms: Exposure to stress increase significantly ($p < 0.001$) the time spent in closed arms, however, post-exposure to music increases this time as like in one controls expect in group exposed to combined stress when the time spent in closed arms remains increased.

DISCUSSION

In this work, exposure to the combined predator and noise stress promoted behavioral and hormonal alterations, including hypersecretion of ACTH and appearance of anxiety in rat, these changes were alleviated by post-exposure to classical music. Increase ACTH level upon exposure to stress is very known as response to the activation of HPA axis [16]. In Elevated Plus Maze, we have shown decrease in the time spent in open arms. The decreased venturing into the open arms in the elevated plus maze is typically interpreted as an increase in anxiety [17]. Hyperactivity of HPA axis was found to be linked to the increase of anxiety [5]. Interestingly, post-exposure to music enhances the anxiety symptoms and secretion of ACTH. The power of music in anxiety tests has been argued in the rat. Lemercier [18] concluded that environmental enrichment, such as by short-duration music, decreases the rat's reactivity in housing spaces but only has a little influence when rats are taken out to be handled and has no influence on the results obtained during an anxiety test. However, Rauscher [19] show a neurophysiological basis for a Mozart effect in rats to complete a T-maze more quickly if they had been reared listening to a Mozart piano sonata, a conclusion that is contested by Steele [20], who argued that the rats were deaf to most of the notes of the sonata. However, exposure to Mozart's music early in life can increase BDNF (Brain-derived neurotrophic factor) concentration in the hippocampus in rats [21, 22]. Finally, we can conclude that music is effective to reduce anxiety and HPA axis activation.

REFERENCES

1. Jian Goa, Y., Y. Xia, S.J. Dai, G.Z. Fang, H. Guo and D.Z. Yao, 2009. Enhancement of Spatial Learning- Memory in developing rats via Mozart Music. *Journal of Electronic Science and Technology of China*, 7: 47-49.
2. Das, A., D. Rai, M. Dixit, G. Patil and C. Nath, 2002. Effect of unpredictable stress on cognition and brain acetyl cholinesterase activity in adult and aged mice. *Indian Journal of Pharmacology*, 34: 416-421.
3. Kim, J.J. and D.M. Diamond, 2002. The stressed hippocampus, synaptic plasticity and lost memories. *Nature Reviews Neurosciences*, 3(6): 453-462.
4. Selye, H., 1936. A syndrome produced by diverse noxious agents. *Nature*, 32: 138.
5. Cannon, W.B., 1932. *The Wisdom of the Body*, Norton, New York.
6. Pacak, K., M. Palkovits, I.J. Kopin and D.S. Goldstein, 1995. Stress-induced norepinephrine release in the hypothalamic paraventricular nucleus and pituitary-adrenocortical and sympathoadrenal activity: *in vivo* microdialysis studies. *Front Neuroendocrinology*, 16: 89-150.
7. Toumi, M.L., S. Merzoug, B. Baudin and A. Tahraoui, 2013. Quercetin alleviates predator stress-induced anxiety-like and brain oxidative signs in pregnant rats and immune count disturbance in their offspring *Pharmacology, Biochemistry and Behavior*, 107: 1-10.
8. Fizza, N., S. Haider, Z.T. Batool, J. Perveen, D. Haleem, 2012. Sub-chronic exposure to noise affects locomotor activity and produces anxiogenic and depressive like behavior in rats. *Pharmacological report*, 64: 64-69.
9. Begoña, E., I. Quero, F. Montserrat, T. Inmaculada, P. Montilla and T. Isaac, 2014. Role of noise and music as anxiety modulators: Relationship with ovarian hormones in the rat. *Applied Animal Behaviour Science*, 152: 73-82.
10. Koelsch, S., 2010. Towards a neural basis of music-evoked emotions. *Trends in Cognitive Sciences*, 14: 131-137.
11. Cruz, J.G.P., D.D. Dal Magro and J.N. Cruz, 2010. Effects of classic music as part of environmental enrichment in captive *Mus musculus* (Rodentia: Muridae). *Biotemas*, 23(2): 191-197.
12. Wells, D.L. and R.M. Irwin, 2008. Auditory stimulation as enrichment for zoo-housed Asian elephants (*Elephas maximus*). *Animal Welfare*, 17(4): 335-340.
13. Nakamura, T., A. Tanida, H. Nijima, J. Hibino, M. Shen and K. Nagai, 2000. Auditory stimulation affects renal sympathetic nerve activity and blood pressure in rats. *Neurosciences Letters*, 416(2): 107-112.
14. Reed, H.J., L.J. Wilkins, S.D. Austin and N.G. Gregory, 1993. The effect of environmental enrichment during rearing on fear reactions and depopulation trauma in adult caged hens. *Applied Animal Behavioral Science*, 36(1): 39-46.
15. Pellow, S.P., S.E. Chopin and M. File, 1985. Validation of open: closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. *Journal of Neuroscience Methods*, 14: 149-67.

16. Patin, V., B. Lordi, A. Vincent and J. Caston, 2005. Effects of prenatal stress on anxiety and social interactions in adult rats. *Developmental Brain Research*, 160: 265-74.
17. Djordjeviæ, J., G. Cvijiæ and V. Davidoviæ, 2003. Different Activation of ACTH and Corticosterone Release in Response to Various Stressors in Rats. *Physiological research*, 52: 67-72.
18. Leonardo, E.D. and R. Hen, 2008. Anxiety as a developmental disorder. *Neuropsychopharmacol.*, 33: 134-140.
19. Lemerrier, H., 2000. Environmental enrichment: music, day and dusk, how do they influence the rat's behaviour in laboratory *rattus norvegicus* 7. *STAL* 25: 23-30.
20. Rauscher, F.H., 2006. The Mozart effect in rats: response to steele (Note). *Music Perception*, 23: 447-453.
21. Steele, K.M., 2006. Unconvincing evidence that rats show a Mozart effect (Note). *Music Perception*, 23: 455-458.
22. Marzban, M.A., M. ShahbaziTondar, M. Soleimani, M. Bakhshayesh, A. Moshkforoush, M. Sadati, S.A. Zendehrood and M.T. Joghataei, 2011. Effect of Mozart music on hippocampal content of BDNF in postnatal rats. *Basic and clinical Neurosciences*, 2: 21-26.